EXCHANGE

OXFORD BLOOD GROUP

THE NEWSLETTER OF THE OXFORD BLOOD GROUP

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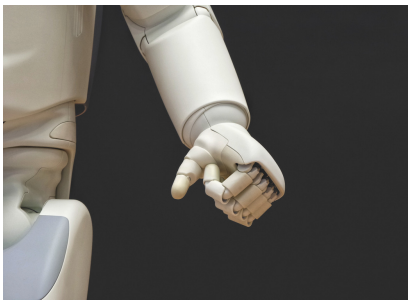
OPPORTUNITIES COMING UP

HAEMATOLOGY DEPARTMENT: PLANS FOR THE FUTURE



The Haematology Department is planning a future redevelopment of services on the existing Churchill site. This may include new building work, and the provision of new spaces for treatment and outpatient clinics. It will be critical to ensure that the site is planned in partnership with haematology patients, and with an understanding of the experiences and views of the people who use the service. The department is planning extensive consultation exercises with people across haematology over the coming months, so look out for opportunities to contribute. We look forward to hearing your views and comments. If you are interested in being involved in future development plans - such as becoming part of a stakeholder group, coming to meetings or sharing your thoughts - please email Catriona on OxfordBloodGroup@ouh.nhs.uk

IN THIS ISSUE

WHAT HAVE WE BEEN UP TO?

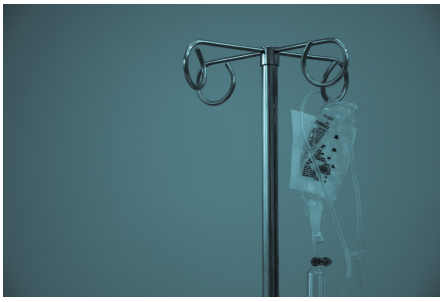
ADVISORY GROUP FOR RT DECISION AID

"The discussion we had last week has prompted me to consider lots of aspects of the work which I hadn't previously thought about – having your perspective was invaluable"

Dr Rebecca Shakir

Oxford Blood Group members have formed an advisory committee to help design a decision aid for people offered radiotherapy for Hodgkin lymphoma. The aid will give people information about how radiotherapy might affect their health later in life. Our first meeting helped the researcher, Dr Rebecca Shakir, to understand how the tool will fit in with the current patient experience, what sort of information patients might want, and how the tool might aid doctor / patient communication. We look forward to working with Rebecca for the duration of her project.

FOCUS GROUP HELPS NEW T CELL LYMPHOMA TRIAL GET THROUGH 'TO THE NEXT ROUND'



Oxford Blood Group members participated in a focus group to discuss a planned new clinical trial for peripheral T cell lymphoma. The trial will use a new agent in combination with chemotherapy as a first line treatment. We were joined by Dr Graham Collins who will be a principle investigator, and representatives from the Southampton Clinical Trials Unit, who are co-investigators of the study.

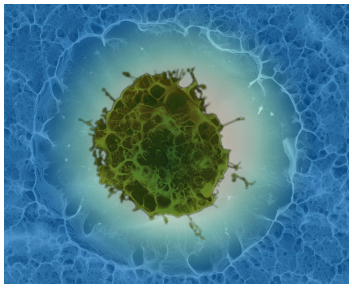
We discussed whether the trial would address questions of importance to people with lymphoma, and whether people would be willing to take part in it. Much of the discussion concentrated on the information that people would want before deciding whether or not to take part, including why randomisation would be necessary (see article page 4-5 of this newsletter), and the practical implications of trial participation, which can incur extra expenses.

> It was great how engaged [people] were and that there were both patients and carers so that we could hear experiences of both in relation to the trials they have been on or their partner was on... the feedback was so good.
> I was inspired by your group and am looking to do something similar in Southampton for each of the portfolios I cover.
>
> Kelly Cozens, Senior Trials Manager, Southampton Clinical Trials Unit

Our input meant that the sponsors could submit their application to Cancer Research UK (CRUK) with a better appreciation of how the trial would be received by patients, and the design of the trial will be influenced by our contribution. The sponsors are 'through to the next round, and will be submitting a full application

CRUK recognised the positive approach to PPI and:
"praised the level of detail provided in the application regarding the impact PPI activity has had on the study."

IMPROVING DONOR STEM CELL TRANSPLANT: QUALITATIVE INTERVIEWS INFORM DESIGN OF NEW RESEARCH STUDY



Oxford Blood Group members and close family members helped with the design of a study to improve the success of donor stem cell transplants. The study aims to test whether giving donors a combination of tablets before they donate will boost important white blood cells (T reg cells) in the donated stem cells.
The scientists suspect that more T reg cells will mean better outcomes for transplant recipients. The researchers needed to question people who had experience of stem cell donation, to ask if the research was important and feasible. Our advice was that the research is hugely valuable, but that some of the practical details of the study would make it impractical for likely participants. The study design has been significantly altered as a result.

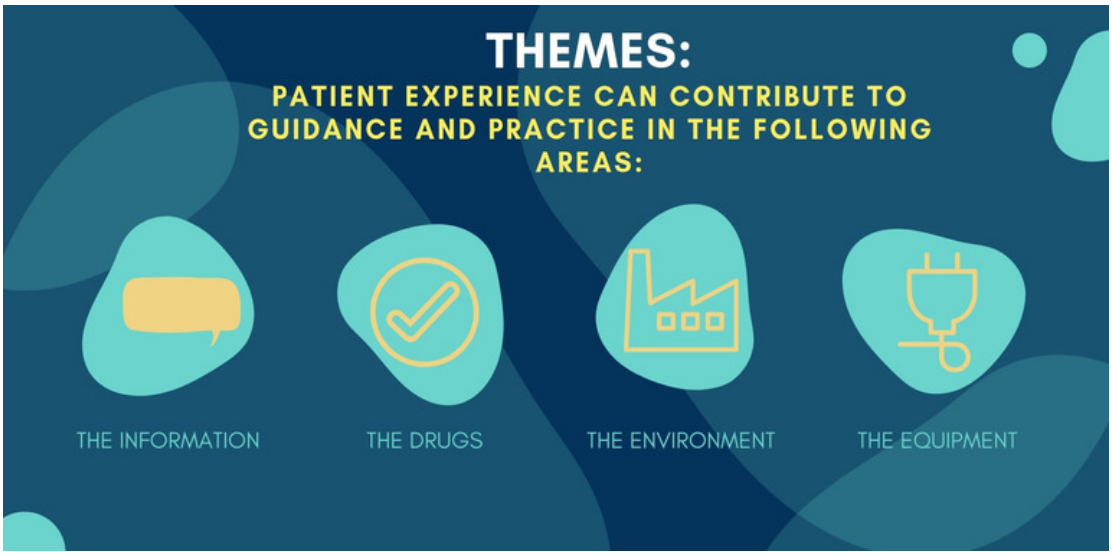
> This exercise was instrumental in providing direct and open comments and responses from relatives of HSCT patients. The positive feedback regarding the aims of the study were encouraging. Most importantly we were able to consider the issues important to HSCT donors that included improving the detail regarding side effects of the intervention and reducing the need for volunteers to visit the OUH Trust premises...the grant application has been strengthened by completing this exercise.
>
> Dr Abigail Lamikanra, NHSBT, OUH

WHAT HAVE WE BEEN UP TO?

BONE MARROW BIOPSY - LEARNING FROM PATIENT EXPERIENCE

Oxford Blood Group members have taken part in two workshops this year to talk about experiences of bone marrow biopsy - and the meetings were a lot more enjoyable than that sounds! At our first meeting, people with both good and bad experiences of bone marrow biopsies discussed how their experiences might be instructive and useful to others. Common ideas were grouped under four themes that indicate how experience might translate into learning.

the treehouse - our home for the workshops



At our second workshop, we discussed the information provided to people who are having a bone marrow biopsy. Pip Doling, who runs the bone marrow biopsy clinic, talked to us about how things work when organising the list, and what information people might want that they are not getting at the moment. It was agreed that we could make substantial contributions to the revision of the existing leaflet, such as references to gas and air, and advice about getting home. We also propose drafting supplementary information about what patients might find helpful.

There are implications for medical training, too, and we will be working with medical colleagues to share the insight from patient experience. For example, doctors might be surprised to learn that most patients don't understand why a bone marrow biopsy is necessary, and why the same information cannot be found from a blood test.

And we have also agreed to ask the department to consider the introduction of a new device for taking bone marrow samples, that makes the procedure less painful and allows the collection of superior samples. The departmental governance meeting has agreed that this is a valuable change in practice, which will be implemented over the coming months.

WHY DON'T WE USE 'HISTORICAL CONTROLS' IN CLINICAL TRIALS?

Readers will probably be familiar with the concept of 'randomisation.' This is a process used in clinical trials that sorts people into different groups at random - it can feel like the roll of a dice.

A typical example of the use of randomisation is the comparison of a new treatment with standard therapy. So, for example, a clinical trial testing a new drug will randomise trial participants into two groups: one group gets the new drug, and the other group has the treatment that is currently the standard – the "control group." The two groups are compared to see whether the new drug is an improvement.

People at PPI events recently have asked why this is necessary. For some people, it might be a disappointment to take part in a trial and not get access to a new drug. Why can't they just give everyone the new drug, and compare what happens with what we already know about people treated with standard therapy (also known as "**historical control groups**")? If we have been using a treatment for a long time, surely we know enough about how well it works to avoid the necessity of measuring it again? And surely there must have been trials about standard therapy that can give you the information you need?

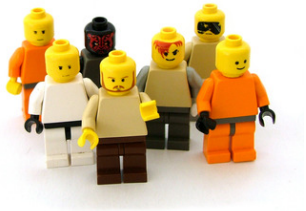
We decided to ask **Dr Graham Collins** to explain why randomisation is necessary:

So-called historical controls are difficult to use and produce unreliable results.

For a start, it is very difficult to use data about the patients that you see routinely in clinic. These patients might not have the same tests, or might not have them at the same time. They might be followed up for shorter lengths of time and they may have better or worse prognosis disease that the group used in the trial. So you can't get the information you need to make a reliable comparison with people getting a new treatment.

That leaves comparisons with clinical trial patients from the past. Clinical trials have strict eligibility criteria. These are rules that govern who can take part and who cannot. They ensure that the people in the trial are as similar to each other as possible. Examples include trials that will not recruit people with other serious medical problems, or people with particular blood results. People in a historical control group from an earlier clinical trial will be selected using different eligibility criteria, meaning that a historical group might be very different to the group you want to test. It's a bit like comparing apples and pears. This makes the effect of the new treatment much more difficult to measure.

"comparing with past clinical trials is a bit like comparing apples and pears: it's hard to tell whether the trial treatment really makes a difference"



randomisation creates two groups that are very similar to each other - which leads to much more reliable results

Small clinical trials with, say, fewer than 200 patients, will not be open in that many hospitals, so there will be a skewing towards certain groups of people on the basis of socioeconomic status or ethnic origin. It is difficult to make adjustments to take account of this.

Diagnostic techniques are improving all the time, which makes it difficult to use information from clinical trials of the past. More recent trials may include people who were diagnosed sooner than those who were in trials from an earlier date. This might make a difference to what happens to the patients in the trial, so if you are combining data from the past you will have really significant differences between groups of people that are difficult to account for.

Perhaps most importantly supportive care is improving all the time.

Supportive care refers to the drugs that people are given to help with chemotherapy treatment, such as antibiotics and growth factors. This has a big impact on what happens to patients. Over the years, the outcomes for some diseases have improved considerably even though the treatment itself has not changed a great deal. So, you can't use data from past trials because those people were having different supportive care. If the patients of today are having better supportive care, how do we know how much of a difference that makes, and how much is due to the trial treatment?

Randomisation is a way of designing a trial that takes account of the inevitable differences between individuals to ensure that the study compares like with like. That makes it much clearer for researchers to tell how much difference a trial treatment really makes.

being part of a trial steering committee (TSC)

There are multiple ways in which patients and the public can get involved in research. One option is to become part of a trial steering committee (TSC). TSCs should include at least one member with experience of the condition being investigated, or a member of the public

The NIHR (National Institute for Health Research) describes the main responsibilities of the TSC as follows:

- to provide advice to those parties involved in organising and running the trial on appropriate aspects of the project
- to monitor trial progress and adherence to the trial protocol
- to consider new information of relevance to the research question
- to ensure the safety of the participants. The rights, safety and well-being of the participants are the most important considerations - more important than the interests of science and society
- to ensure that the trial has been approved by the necessary committees
- to agree any substantial changes to the way the trial is run.

- You should be given clear instructions about your role and what will be expected of you. Sometimes extra training will be available.
- You should expect that meetings will be conducted using language that is clear to a lay person.
- You should be told how much time will be involved, how frequently you will be needed at meetings and where meetings will take place
- Bear in mind that a lot of time is taken up reading papers prior to a meeting
- Meetings might be some distance from home - factor in time taken off work or away from family commitments
- There will be an agreed payment scheme to reimburse you for time and expenses, and this should be clearly stated from the outset.

Spotlight on Oxford Haematology Research

"Clinical trial outcomes in haemorrhage research"

When you think of research, you might think of laboratories or clinical trials or new treatments. But sometimes researchers do research to find out how to improve research – such as in this recently published scientific paper.

Brenner *et al. Trials* (2018) 19:533
https://doi.org/10.1186/s13063-018-2900-4

Trials

COMMENTARY Open Access

Outcome measures in clinical trials of treatments for acute severe haemorrhage

Amy Brenner[1*], Monica Arribas[1], Jack Cuzick[2], Vipul Jairath[3], Simon Stanworth[4,5,6], Katharine Ker[1], Haleema Shakur-Still[1] and Ian Roberts[1]

Readers may have heard references to "outcome measures" of clinical trials. Outcomes are the things that happen to the people in the trial; researchers measure trial outcomes when deciding how to interpret trial results. But there are multiple ways to measure outcomes, and the choice of outcome has an important impact on how a trial is interpreted. A group of scientists, including Dr Simon Stanworth from the Transfusion Medicine team in Oxford, recently evaluated what outcome measures should be used when considering different treatment options for acute severe haemorrhage.

Acute severe haemorrhage is a life-threatening complication of trauma, childbirth, and surgery. Different clinical trials have evaluated a number of interventions to reduce blood loss. In this paper, the researchers pooled the data from 3 clinical trials to assess the best outcome measures. The trials studied were CRASH-2 (haemorrhage as a result of trauma), WOMAN (haemorrhage after delivery of a baby), and HALT-IT (haemorrhage from bleeding from the gut).Most trials for treatment of acute severe haemorrhage measure an outcome called "all-cause mortality."

This means that the success of the treatment is determined by measuring what proportion of the trial participants die, regardless of what causes death. However, studies have shown that a significant proportion of the people in these situations die because of complications that are not related to the bleeding. These might include infection, or a complication due to another medical condition. If only all-cause mortality is measured, the data from the trial might be misleading.

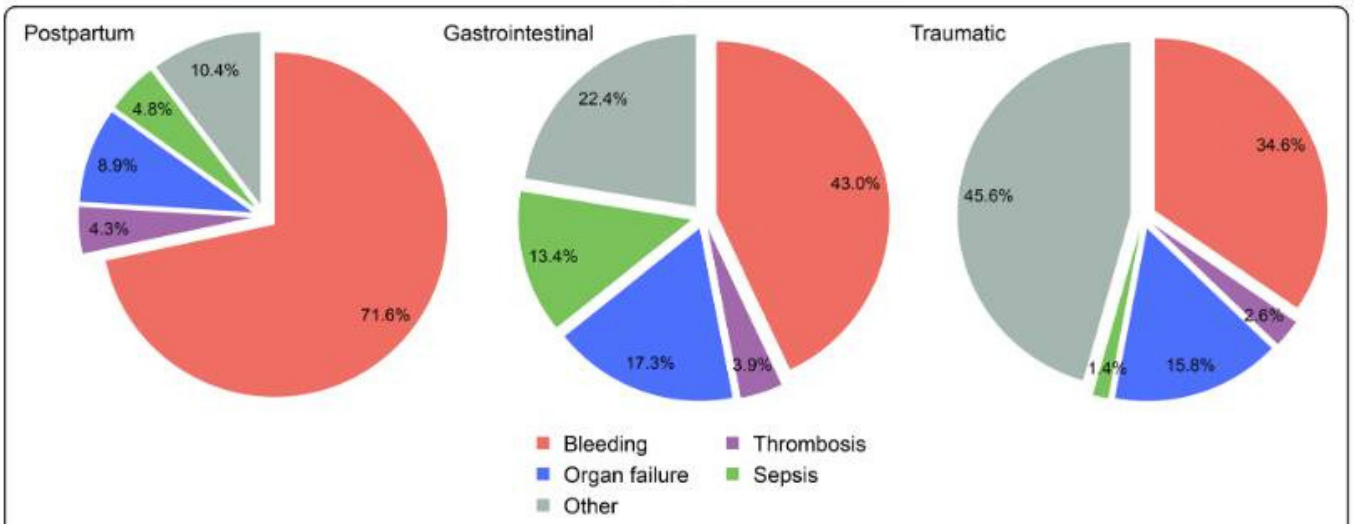


Fig. 1 Primary cause of death by site of acute severe haemorrhage. Other causes of death in traumatic haemorrhage include head injury (39.8%). Other causes of death in gastrointestinal haemorrhage include cancer (10.3%) and liver disease (2.3%). Other causes of death in postpartum haemorrhage include eclampsia (2.1%) and pulmonary oedema (1.5%)

By re-analysing the data from all 3 of these trials, the researchers were able to conclude that using all-cause mortality reduces the chance of determining the actual benefit of the medication's action. It makes it difficult to apply the conclusions from the trial to the care of people who experience haemorrhage. And finally it can even mask potential harmful events due to the medication being studied. They make the point that "because death is important to patients, easy to quantify and may be affected by treatment, it is an important outcome measure in clinical trials in life-threatening bleeding." However, the conclusion from this current paper is that future clinical trials should not be designed to measure all-cause mortality, but should focus specifically on mortality due to the bleeding itself. By measuring things in different ways, the results of a trial are much more reliable and more useful to doctors and patients.

At Oxford Blood Group, we take particular interest in clinical trial design, to ensure that patients are involved from early stages in planning a trial. This involvement includes making sure that trial outcomes that matter to patients are evaluated. Please get in touch if you would like to find out more about contributing to clinical trial design.

TRAINING & MEDICAL CONFERENCES: GETTING PATIENTS ON THE PODIUM

We are thrilled that some of our members will be sharing their experiences on the podium at forthcoming academic and training events for haematologists.

At the annual meeting of the Oxford Centre for Haematology - an event that attracts prestigious global contributors - one of our members will talk to the audience about PPI: her experience, what it has meant to her and what engaging with patients can bring to the practice of haematology.

And then we will welcome four of our members to an annual Lymphoma Masterclass course for haematology registrars at Keble College, to appear in conversation with Dr Graham Collins. The small group will share stories from their own experience to illustrate what makes a great doctor, and to share the things that matter most to patients with the future generation of lymphoma specialists.

WORLD Sickle Cell DAY JUNE 19

June 19th is World Sickle Day. There are 12,000 people living with sickle cell disease in the UK. Sickle cell disease affects people from Afro-Caribbean backgrounds and is a genetic disorder inherited as a recessive condition (this means each patient inherits one copy of the defective gene from each parent). People with sickle cell disease suffer from painful crises- debilitating pain usually felt in the limbs.

Q- What can I do to help people with sickle cell disease?
A- Become a blood donor!

Give Blood

and lastly...

We are an involvement and engagement group for anyone with experience of a haematological illness. Your experience gives you a perspective that can be valuable in research and service improvement.

But, we need our professional colleagues and researchers to get involved with us too - so get in touch with any project that would benefit from involving patients.

a **BIG**

to all of those who have helped with our work so far.